

Title: An Inhaler

The present invention relates to an inhaler according to the preamble of claim 1. Such an inhaler is useful for a one-time-use-and-dispose-means for supplying a dose
5 of an active, inhalable, particulate substance.

Technical Background

WO 96/22802 discloses an inhaler of the above-mentioned type for pulmonary inha-
10 lation comprising a tubular body in which an air flow passage is defined. The inhaler comprises only a single dose of an active, inhalable, particulate substance arranged within the air flow passage, said dose being sealed or closed in relation to the ambi- ent atmosphere by closure means which are to be removed or opened by a user prior to use, the inhaler being intended to be used only once. WO 98/53869 discloses a
15 similar tubular body for nasal inhalation.

The closure means of the known inhaler can be caps at each free end of the tubular body, either as two separate caps or as a two integrated twin caps, in case the tubular body is bent to a position with the free ends closely adjacent.

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The single dose contained in the inhaler is a particulate material, normally including one or more pharmaceutically active agents, if appropriate, together with conventional pharmaceutically acceptable additives. In the known single dose inhaler, the particulate material often has a volume substantially smaller than the inner volume
25 of the inhaler between the two caps. Because the volume of said particulate material is substantially smaller than the inner volume of the inhaler, said particulate material may be moved and shaken in the inhaler tube during transport and storage, which at least in case of certain preparations, may lead to alterations of particle size, composition of the particulate substances due to segregation, disintegration and crumbling.
30 Further, it is possible that mechanical impact such as shaking will cause the individual grains of the particulate material to stick together or to the inner walls of the tu-

bular body, thus yielding undesired mechanical properties or incorrect dosage. Such alterations may change the inhalation behaviour of the particulate material, jeopardizing the correct administration of the pharmaceutical agent.

5 Summary of the Invention

The object of the invention is to provide an inhaler of the above type, in which the above problems are substantially reduced or fully eliminated. This is obtained by an inhaler according to the characterising clause of claim 1. By having the inhalable, particulate substance in a cap, two objects are obtained. Firstly, the tubular body with the corrugations may be used for dispensing inhalable, particulate substances of an unspecified type, and a generic store of these may be maintained by a user, a pharmacist, a hospital, etc. It is therefore just a matter of attaching the cap including a specific, inhalable, particulate substance to the tubular body and dispense the inhalable, particulate substance into the tubular body. Secondly, by having the inhalable, particulate substance in the cap, it is easier to prevent movement of the inhalable, particulate substance, thus reducing or preventing alterations to it. The essential feature, however, is that the particulate substance is supplied so as to be positioned at the beginning of the corrugated section before inhalation. As a result, the lumps of the particulate substrate due to the hittings of subsequent corrugations before inhalation will be crushed and dispersed more and more into finer particles every time they hit one of the succeeding corrugations. As a result, a far more improved powder dispersion is obtained than hitherto known, the fraction of respirable particles being increased.

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According to the invention the cap may comprise at least one closed compartment containing the active, inhalable, particulate substance, the tubular body or said cap comprising means for dispensing said at least one particulate substance by opening, breaking or piercing said at least one closed compartment. Having one or more closed compartments in the cap, it is possible to supply one or more pharmaceutically active agents, which can or cannot be stored together. Further, means are pro-

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vided, said means being capable of opening the closed compartment and thus facilitating the dispensation of said agents into the tubular body at the beginning of the corrugations.

5 Furthermore, according to the invention the cap may comprise at least one attachable part comprising at least one closed compartment containing an active, inhalable, particulate substance. In this manner, a combination approach can be used where several, different, pharmaceutically active agents may be used for a single treatment.

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Moreover, according to the invention the at least one closed compartment may be closed by means of a tear-off foil, said tear-off foil being adapted to be removed after the at least one attachable part is attached to the cap. By closing the compartment by means of a tear-off foil, and adapting the tear-off foil to be removed after the at
15 least one attachable part is attached to the cap, the risk of contamination is reduced, and the closed compartment is easily opened for dispensing.

Further, according to the invention the at least one closed compartment may be closed by means of a slidable element with at least one hole, in which said slidable
20 element has a first and a second position, said slidable element in said first position being adapted to close said closed compartment, and in said second position being adapted to open said closed compartment by communicating said closed compartment with said hole, said slidable element comprising friction elements adapted to hold said slidable element in the first position to produce some friction, while said
25 slidable element is moved from said first position to said second position, said slidable element being fixed at said second position. When the closed compartment is closed by the slidable element, the compartment can easily be opened for dispensation, simply by applying pressure thereto, e.g. by the use of the thumb and index finger. The slidable element may be provided with special pads for applying the
30 pressure. By adding friction elements, e.g. in the form of roughening surfaces or a hole/pin-arrangement it is possible, on the one hand, to secure that the closed com-

partment is not accidentally opened, and, on the other hand, to ensure that a used cap is not accidentally reused.

Further, according to the invention the closed compartment may be closed by a
5 pierceable foil, the tubular body being adapted to pierce said foil, when the cap is attached to said tubular body. The tubular body may be adapted to pierce the foil, e.g. by cutting it at an angle much like the straws used by cartons for juice and chocolate milk.

10 Further, according to the invention the closed compartment may be closed by attaching the cap to the tubular body and bending said tubular body, said closed compartment being opened by unbending said tubular body, and means being provided to keep the tubular body bent, while not in use. Bending the tubular body causes a portion of the tubular body to be squeezed off and creates a closed compartment at the
15 end.

This closed compartment may then be reopened simply by straightening the tubular body. By providing means for keeping the tubular body bent, an accidental dispensation of the inhalable, particulate substance is prevented.

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Further, according to the invention the closed compartment may be closed by providing means squeezing together a part of the tubular body, said closed compartment being opened by removing said means. The means squeezing the tubular body may be in the form of a clothes pin, a fork or other.

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Further, according to the invention the closed compartment may comprise a tube-like body, one end of which being permanently closed, while the other end being adapted to be inserted into the tubular body, said closed compartment being closed by means sticking a part of the walls of said tube-like body together, said closed
30 compartment can be opened by adding pressure to or pulling at said tube-like body. The one end of the tubular body is permanently closed by glue, welding, melting or

other means ensuring no reusable force to open it. The walls are stuck together in such a manner that if pressure is applied thereto, e.g. from the thumb or index finger, the compartment will open.

5 Further, according to the invention the at least one closed compartment may be closed by means of a rotating, slidable element with at least one hole, said rotating, slidable element having a first and a second position, and said rotating, slidable element in said first position being adapted to close said closed compartment, and in
10 said second position being adapted to open said closed compartment by communicating said closed compartment with said hole, said rotating, slidable element comprising friction elements, said friction elements being adapted to hold said rotating, slidable element in the first position to produce some friction, while said rotating, slidable element is rotated from said first position to said second position and fixate
15 said rotating, slidable element at said second position. When the closed compartment has a rotating, slidable element, a simple screw-like motion will open the closed compartment. Likewise with the slidable element mentioned above, the friction elements provide means against accidental opening of the closed compartment and accidental reuse.

20 According to the invention the cap may be constructed from a soft, squeezable material, and the closed compartment may likewise be constructed from a soft, squeezable material, said closed compartment being adapted to rupture, when pressure is applied to said cap, and the material of the closed compartment being adapted in such a manner that, when it ruptures, the material is not dispensed to the tubular
25 body. In this embodiment the closed compartment is, in many ways, similar to the bubbles in bubble-wrap used in protective envelopes. When pressure is applied to the cap, e.g. with the thumb and index finger, the bubble containing the inhalable, particulate substance and the inhalable particulate substance is dispensed to the tubular body. A special advantage is when the bubble is manufactured with a shaped,
30 weak spot, the bubble will rupture in a known way, and none of the material of the bubbles will end up in the tubular body.

Finally, according to the invention the cap may be adapted to accommodate two or more of the tubular bodies. In this manner, two inhalable, particulate substances can be sucked in at the same time through the mouth.

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Brief Description of the Drawings

The invention will be described below with reference to the examples shown in the drawings, in which

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Fig 1 shows a known inhaler configuration,

Figs 2-4 show a cap with an attachable, closed compartment for an inhaler according to the invention,

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Figs 5 and 6 show a cap with an attachable, closed compartment in an alternative embodiment,

Figs 7-9 show different ways of sealing and opening the closed compartment,

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Figs 10-14 show embodiments, in which the closed compartment is closed by bending the tubular body,

Figs 15 and 16 show an embodiment, in which the closed compartment is created by squeezing together a part of the tubular body,

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Fig 17 shows an embodiment, in which the closed compartment is formed by first closing the outer end of the tubular body by gluing, welding or a similar technique,

30 Figs 18 and 19 show an embodiment similar to the one shown in Figs 5 and 6,

Fig 20 shows an embodiment, in which the closed compartment is designed to rupture,

Fig 21 shows the weakened area of the closed compartment seen from below, and

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Figs 22 and 23 show an inhaler assembly comprising more than one inhaler according to the invention,

Fig 24 shows an inhaler having a cap with a weld-on foil in both ends,

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Fig 25 shows a cap having two closed compartments, and one tear-off foil for each compartment,

Fig 26 shows a cap having two closed compartments, and a common tear-off foil or

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both compartments,

Figs 27a, 27b and 27c show the flow through the corrugated middle section of the tubular body,

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Fig 28 shows an inhaler for pulmonary and nasal inhalation,

Fig 29 shows an inhaler for pulmonary or nasal inhalation together with a closed compartment including a pill to be swallowed separately, and

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Fig 30 shows an inhaler having a cap with a closed compartment including a pill to be swallowed separately.

Detailed Description

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As shown in Fig 1, the known inhaler comprises a tubular body 1 and a cap 2. The tubular body 1 has a corrugated middle section 3 creating a whirl chamber and al-

lowing it to be bent at an angle. The corrugations are substantially saw-tooth formed. The inhaler may be used as a pulmonary inhaler or as a nasal inhaler. If it is used as a nasal inhaler, one end of the tubular body 1 should be easily inserted into the mouth and the other end into one nostril of a patient. Simply by blowing through
5 the tubular body 1, the contents of the tubular body 1 will enter the nose.

The cap 2 shown in Fig 2 for an inhaler according to the invention has a closed compartment 4 containing a pharmaceutically active agent in the form of an inhalable, particulate substance. As mentioned above, transport and handling of the in-
10 haler may cause unwanted effects to sensitive components on the particulate substance. Having the particulate substance in a small closed compartment 4 as illustrated in Fig 3, much of the mechanical agitation of the particulate substance is prevented, thereby reducing or eliminating the adverse effects. When the cap 2 is placed on the tubular body 1, means 10, 11 are provided for opening the closed
15 compartment 4 and for dispensing the particulate substance into the tubular body 1 at the beginning of the corrugations ready for inhalation.

As shown in Fig 2, the closed compartment 4 may be provided as a separate unit attachable to the cap 2 by attachment means 5, 6. These attachment means 5, 6 fix the
20 closed compartment 4 in place, usually in a non-removable manner. This has the advantage that the pharmaceutically active agent can be supplied separately, and one inhalator may be used for many different medications. The closed compartment 4 has an inner space 7 and an opening 8 as shown in Fig. 3. The inner space 7 is then filled with the particulate substance, and means are provided for closing and opening
25 the closed compartment 4. The attachment means 5, 6 of the closed compartment 4 matches the cap 2, and when the closed compartment 4 is opened, the opening 8 of the closed compartment 4 is in communication with an opening 9 of the cap 2, allowing the particulate substance to be dispensed into the tubular body 1.

The general principle of the inhaler according to the invention has now been described. What remains to be described are ways by which the closed compartment 4 is closed and opened in use.

- 5 As shown in Fig 2, one embodiment of the closed compartment 4 is closed by a tear-off foil 10. This tear-off foil 10 is composed of a laminate barrier foil such as a layer of aluminium covered by a layer of polypropylene on both sides, said tear-off foil 10 being attached to the opening 8 of the closed compartment 4 shown in Fig. 3. By pulling at the foil 10, which is bent 180°, said foil is separated from the opening 8,
10 and the opening 8 of the closed compartment 4 is in communication with the opening 9. The tear-off foil 10 is provided with an end 11, allowing the foil 10 to be torn off, when the closed compartment 4 is attached to the cap 2 simply by pulling at the end 11.
- 15 As a result the particulate substance in the closed compartment 4 is protected against moisture without needing additional packaging for moisture protection, which is of importance to moisture sensitive formulations.

- Figs 5 and 6 show a cap with an attachable, closed compartment in an alternative
20 embodiment consisting of two portions, a lower portion and an upper portion. The lower portion is to be mounted on the U-shaped inhaler tube and the upper portion with the closed compartment including the particulate substance is to be clipped to the lower portion by means of extending hooks on the lower portion, said hooks engaging corresponding notches in the upper portion. The particulate substance is re-
25 leased by removing the tear-off foil. This embodiment is better suited for mass production than the embodiment shown in Figs 2-4.

- Figs 7 and 8 show an embodiment, in which the closed compartment 4 is closed by a slidable element 12 with a hole. In a first position, the slidable element 2 closes the
30 closed compartment 4, and in a second position the hole 13 of the slidable element 12 is in communication with the closed compartment 4, allowing the particulate sub-

stance to be dispensed. The slidable element 12 can be provided with means for pushing it or, as shown, be moved by pushing the cap 2 and the closed compartment 4 together in the direction of the arrows 14. Alternatively, the closed compartment 4 may be opened by pulling the cap 2 and the closed compartment 4 apart. The cap 2 and the closed compartment 4 may be provided with means for helping and pushing them together, e.g. in the form of push-pads, or the like. The slidable element 12 may be provided with friction elements, e.g. in the form of roughened surfaces or by providing pins and holes, locking the cap 4 and the slidable element 12 together and requiring an amount of force to overcome. This has the advantage that the risk of accidental opening of the closed compartment 4 is lessened and prevents accidental re-use of a cap 2.

Fig 9 shows an embodiment, in which the closed compartment 4 is closed by a piercable material 14. When the cap 2 is attached to the tubular body 1, the end 15 of the tubular body 1 pierces the piercable material 14. The piercing of the piercable material 14 may be helped by shaping the end 15 of the tubular body 1, e.g. by making a diagonal cut to it. This is not unlike how a straw pierces the membrane of a juice carton.

Figs 10-14 show embodiments, in which the closed compartment 4 is closed by bending the tubular body 1 and thereby squeezing off a part thereof. The closed compartment 4 is then opened simply by straightening the tubular body 1 in the direction of the arrow 16. The tubular body 1 is provided with means 17, 18 for keeping the tubular body 1 bent while not in use, e.g. by a fastening device 17 holding the ends of the tubular body 1 together or by placing the tubular body 1 in a holder 18, maintaining the bent position.

Figs 15 and 16 show an embodiment, in which the closed compartment is created by squeezing together a part of the tubular body 1 by using a squeezing device 19. When the squeezing device 19 is pulled in the direction of the arrow 20 afterwards, the closed compartment 4 opens.

Fig 17 shows an embodiment, in which the closed compartment 4 is formed by first closing the outer end of the tubular body 1 by gluing, welding, melting or a similar technique. An outer seal 21 is created and can only be broken by tearing the material of the tubular body 1. A bit further along the tubular body 1 a second seal 22 is created. This seal 22 is weaker than the outer seal 21 and can be opened by applying force in the direction of the arrows 23. This force can be created by applying pressure, e.g. with the thumb and index finger, in a plane perpendicular to the plane of the paper.

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Figs 18 and 19 show an embodiment almost similar to the one shown in Figs 5 and 6. The difference is that the motion is a rotating rather than a translating, and the closed compartment 4 is opened by twisting the cap 2.

Fig 20 shows an embodiment, in which the cap 2 and the closed compartment 4 are constructed from a soft, squeezable material. When pressure is applied to the cap 2, e.g. with the thumb and an index finger, the closed compartment 4 is designed to rupture, allowing the particulate substance contained therein to be dispensed to the tubular body 1. In this embodiment the design of the closed compartment 4 is not unlike the bubbles used in bubble-wrap for protective envelopes.

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Fig 21 shows the closed compartment 4 from below. The closed compartment 4 may be provided with a special weakened area 24, ensuring rupture of the closed compartment 4 in a known manner, and that the material of the closed compartment 4 does not accidentally end up inside the tubular body 1.

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Figs 22 and 23 show a special, multi-tube inhaler comprising more than one inhaler according to the invention. Each of the inhalers can be any of the above types, but the multi-tube arrangement permits inhalation of different pharmaceutically active agents through the mouth, use of larger doses, use of pharmaceutical agents having incompatible storage requirements or any number of other reasons.

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Fig 24 shows an embodiment of an inhaler, in which the closed compartment including the particulate substance is closed by means of both ends of the tear-off foil.

- 5 Fig 25 shows an embodiment of an inhaler comprising a tubular body closed by a cap, part of which being closed by means of one weld-on foil at each end so as to provide two closed compartments, each for the at least one active, particulate substance.
- 10 Fig 26 shows a cap having two closed compartments and a common tear-off foil for both compartments.

This embodiment is suited for integrated medication.

- 15 Figs 27a, 27b and 27c show the flow through the corrugated bendable section of the tubular body after the particulate substance has been released from the cap at the beginning of the corrugations in the intake direction. As a result the lumps of the particulate substance due to the hittings of the step site of the corrugations are crushed and dispersed more and more every time they hit one of the succeeding corrugations.
- 20 As a result a better powder dispersion is obtained than hitherto known, cf the following table, illustrating the influence of the corrugations.

Device corrugation study

- 25 The influence of the localisation of the powder in the whirl chamber was investigated. The selected powder formulation (cf Budesonide formulation study) was respectively located at the beginning (1/3, cf Fig 27a), in the middle (2/3, cf Fig 27b) and at the end (3/3, cf Fig 27c) of the corrugation zone of the device with respect to the outlet portion.

The Fine Particle Dose (FPD) of the delivered dose from each corrugation zone was determined by using the MSLI. Table 1 summarises the test results for each localisation in the corrugation zone.

5 **Table 1 Budesonide corrugation studies**

		1/3 of corrugation zone	2/3 of corrugation zone	3/3 of corrugation zone
Fine Particle Dose (FPD)	< 5µm [µm]	41.9	40.2	49.0
	<5 µm [%]*	26.3	26.3	34.1
Metered Dose (MSLI)	[µg Budesonide]	170.4	165.2	161.5
Delivered Dose (MSLI)	[µg Budesonide]	158.9	152.6	143.8

The percentage refers to the delivered dose detected by MSLI

The conclusion is that:

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- The position of the drug in the device seems to influence the Fine Particle Dose (FPD).
- The higher the number of corrugations touched the better the value for the FPD.

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- Between zone 1/3 and 2/3 no difference was noted.
- Between zone 2/3 AND 3/3 a difference was noted.

The previous devices require the manufacturing equipment to perform pre-filling of the dose into the inhaler tube. According to the invention such handling has been

simplified by instead doing pre-filling into the cap and subsequently sealing the cap. As a result, a higher production speed and lower handling costs have been obtained.

5 The invention has been described by way of several different embodiments. It is possible to make numerous alterations to the embodiments shown and described while staying within the scope of the invention.

The inhaler according to the invention may be used for nasal as well as pulmonary inhalation.

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Fig 28 shows an inhaler for both pulmonary and nasal inhalation. The inhaler comprises a cap with two closed compartments. Each compartment includes an active, inhalable, particulate substance. Each of the substances may be released separately by removing a separate tear-off foil. One of the released substances may be used for
15 pulmonary inhalation. Thereafter, the substance in the other closed compartment may be released to the tubular body to be inhaled by nasal inhalation. As a result, a device for both pulmonary and nasal inhalation has been provided.

One of the tear-off foils may also be provided with a pill to be swallowed in a con-
20 ventional manner.

Fig 29 shows a device for pulmonary or nasal inhalation together with a closed compartment including a pill. The pill and the inhalable, particulate substance may be discharged simultaneously by removing a tear-off foil, which is common for the
25 compartment including the pill and the compartment, including the particulate substance to be discharged into the U-formed tubular body.

Fig 30 shows a device with a cap including a closed compartment for a pill to be swallowed separately.

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